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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,239	07/18/2005	Peter John Sadler	14084-005US1 / RJW/CP6263	5058

23575 7590 07/10/2007

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EXAMINER	
GALLIS, DAVID E	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
07/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,239	SADLER ET AL.	
	Examiner	Art Unit	
	David E. Gallis	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-35* is/are pending in the application.

4a) Of the above claim(s) *16-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/24/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 16 through 35 are pending. Claims 1 through 15 have been cancelled. Claims 16 through 25 have been withdrawn.

Applicant's claim to the benefit of GB 0215526.5, filed on July 5 2002, is recognized and supporting documentation has been received.

Election/Restrictions

2. Applicant's election with traverse of Group II is acknowledged by the examiner. However, the Examiner does not find the argument persuasive. Examiner has reviewed the structure presented by Carmona et al., and finds that the core structure constituting the phenyl and bidentate ligand complex is known, and thereby, can not serve as a special technical feature. The technical feature linking Groups I and II lacks novelty as a Ruthenium (II) compound. Carmona et al. teach a Ruthenium (II) complex wherein with respect to the instant formula (I) of claim 22, R1=isopropyl, R2, R3, R5, and R6=H, R4=methyl, X=halo, T and T'=O, R=H, R1c and R3c=methyl, and m=0 (See Carmona, D. et al, "Synthesis, X-Ray Structure, and Nuclear Magnetic Resonance (1H and 13C) Studies of Ruthenium (II) Complexes containing Pyrazolyl Ligands", J. Chem. Soc. Dalton Trans., 1990:1463-1476 (1990), page 1464, structure (2).) The structure of Carmona directly anticipates the structure of instant claim 22. This demonstrates lack of novelty with respect to the compound claimed. Therefore, a technical feature linking the inventions of Groups I and II does not constitute a special feature as it does not define a contribution over prior art. Since Groups I and II are not linked by the same or a corresponding special technical feature as to form a general inventive concept, the

restriction is maintained and made final. Based on the species election, the scope of examination reading on the elected species are claims 30 formula II-IX, or claim 31 XI-XV, or claim 32 wherein both T and T' are oxygen. Claims 26-29, 33-35 reading on the elected scope will be examined.

Claims 16-25 and the remaining subject matter of claims 26-35 are withdrawn from consideration per 37 CFR 1.142(b).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

4. Claims 26 through 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of ovarian adenocarcinoma for some claimed compounds, does not reasonably provide enablement for the treatment of cancer and/or prevention of cancer in general, or the treatment of adenocarcinoma for all claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

Claim 26, while being enabling for treating ovarian adenocarcinoma using 5 of the 7 exemplary compounds, does not reasonably provide enablement for treating cancer in general through the use of the elected genus of compounds. The ovarian cancer cell line A2780 is specifically an ovarian adenocarcinoma (see Morris et al., page 3620, column 2, line 4). Carcinoma is but one classification among five

recognized cancer catagories (see International Classification of Diseases for Oncology, Third Edition (ICD-O-3)). Claim 26 broadly claims the treatment of cancer, which is outside the scope of enablement for the test results on an ovarian adenocarcinoma cell line. Furthermore, novel cancer drugs are surveyed by the National Cancer Institute (NCI) according to their quantitatively observed inhibitory effects on a multitude of cell lines characteristic of the full range of cancer categorizations (see Grever et al., Seminars in Oncology, 19(6), 12/92, 628, Fig 3). Such a rigorous investigation is not within the scope instant disclosure, and especially in view of the disclosed IC50 values that show no apparent activity for Example No. 2 and no reported test result for Example No. 7. In this field of cancer treatment art, with such a high degree of unpredictability, the very limited examples with inoperability among them lacks sufficient support for the claimed scope encompassing such an enormous number of compounds with diversified structure

Additionally, Claim 26, while being enabling for treating ovarian adenocarcinoma using select compounds of a select bidentate ligand of formula (I), does not reasonably provide enablement for using all claimed ligand types of formula (I). The specification teaches the test results for seven exemplary compounds, all of which can be characterized with Y and Y' as O. Claim 26 broadly claims the use of structures of formula (I) containing Y-L-Y' where Y and Y' are independently selected from O, S and NR^{16}. Clearly the scope of enablement with respect to the charged bidentate ligand is limited to charged oxygen donor groups as the specification is devoid of any data

demonstrating tumor inhibition for formula (I) compounds bearing charged S and N donor functionalities.

Furthermore, Claim 26, while being enabling for selected formula (I) compounds treating an ovarian adenocarcinoma, does not reasonably provide enablement for preventing cancer in conventional sense of the term. Although Applicants specify that "It should be understood that the prevention or inhibition of metastasis is encompassed by 'preventing cancer'", there is no disclaimer to or exclusion of the customary use of the term "prevention". Applicants are not enabled for preventing cancer. The only established prophylactics are vaccines and not the elected Group IV compounds of formula (I) present in the claim. In addition, it is presumed that "prevention" of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who will becoming afflicted.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. 1) As discussed above, preventing cancer requires identifying those patients who will acquire the disease before symptoms occur. This would require extensive and potentially opened ended clinical research on healthy subjects. Likewise treating all types of

cancer, and doing so with unexplored compounds, would require research far beyond the current investigations using these compounds; 2) the third paragraph of page 18 of the specification lists the tumors Applicant intends to prevent and treat, and many different cancer types can associate themselves with these cellular proliferations; 3) There is no working example of such a preventive procedure in man or animal in the specification, let alone examples utilizing all compound types claimed. 4) The claim rejected is drawn to clinical oncology and is therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become afflicted before the fact, nor for determining the efficiencies of untested compounds. Also, no treatment is art-recognized as affective against all five cancer categories. 6) The artisan using Applicants invention would be a Board Certified oncologist with an MD degree and several years of experience, and would also be knowledgeable in synthetic coordination chemistry. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of cancer. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished (In re Ferens, 163 USPQ 609). No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art (Genentech vs. Novo Nordisk, 42 USPQ2nd 1001, 1006). This establishes that it is not reasonable to any agent to be able to prevent cancer generally or treat all cancer catagories. 7) It is well established that "the scope of enablement varies inversely with the degree of

unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The most obvious measure of the instant degree of predictability is the observation that Example No. 2 has little discernable activity relative to the other tested compounds. There is no cited characteristic of No. 2 that lends itself to a predictable inactivity. 8) The claim broadly reads on all patients and all cancers, not just those undergoing therapy for a carinoma and on the limited class of tested compounds embraced by formula I of claim 26.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

6. Claims 26 through 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Regarding claim 26, the term "subject" renders the claim indefinite because "subject" is undefined. In order to facilitate treatment, one generally administers to a "subject in need of treatment". The examiner suggest that the Applicant incorporate this terminology into claim 26 in place of "subject".

8. Claim 26 recites the limitations that the Y-L-Y' is a bidentate ligand bearing a negative charge, and also that the compound comprises a counter ion if charge m is –1 or +1. Given that X may optionally be singularly anionic donor ligand and Y-L-Y' must

carry a single negative charge, then it follows that a countering cation is not a viable limitation, and therefore m=-1 can never exist.

9. Claim 30 recites the limitation "T'"' in formulae (IV) through (IX). There is insufficient antecedent basis for this limitation in the claim. Y-L-Y' bidentate ligands selected from formulae (II) through (X) are not defined to include both T and T' carrying whole charges independently. Thus each of Y-L-Y' formulae (IV) through (IX) are construed to carry a double negative charge, for which, there is no antecedent basis. Furthermore, ligands (IV) through (VIII), as depicted, are incapable of charge delocalization between the T and T' atoms (even assuming a single negative charge). This lack of ability to distribute charge between T and T' atoms also lacks antecedent basis. This claim depends from claim 26 which recites the limitation that "Y-L-Y' is a bidentate ligand bearing a negative charge with a portion of the charge on both Y and Y'".

10. Claim 31 presents the option of formula (XIII). There is insufficient antecedent basis for this limitation in the claim. Dimeric Y-L-Y' bidentate ligand (XIII), as drawn, is incapable of charge delocalization between the T and T' atoms or the T'' and T''' atoms, or even between the two sets of atom pairs. This inability to distribute charge between T and T' atoms and T'' and T''' atoms lacks antecedent basis. This claim depends from claim 26 which recites the limitation that "Y-L-Y' is a bidentate ligand bearing a negative charge with a portion of the charge on both Y and Y'".

Claims 27 through 35 depend from rejected base claim 26.

Claims 26-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The scope of the claims are not understood. Please note that Y-L-Y' was defined to be a bidentate carrying a negative charge, yet nowhere was a position charge noted in formula I. If Y-L-Y' bears a negative charge, it should always be an ionic product which is different from a covalently bounded product. Further without locating the charge and quantity of the positive charge, it is unclear how an M=+1 or m= -1 would occur and what the counter ion would be? Please note formula I contains chemical compounds, a covalently bounded compound or a salt are different classes of compounds which do not share any commonality. It is recommended that explicit structural delineation be defined in the claims commensurate in support of description and enablement from the specification.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David E. Gallis whose telephone number is 571-272-9068. The examiner can normally be reached on Mon-Fri 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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